Citation:

Lindström J, Ilanne-Parikka P, Peltonen M, Aunola S, Eriksson JG, Hemiö K, Hämäläinen H, Härkönen P, Keinänen-Kiukaanniemi S, Laakso M, Louheranta A, Mannelin M, Paturi M, Sundvall J, Valle TT, Uusitupa M, Tuomilehto J; Finnish Diabetes Prevention Study Group. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study.*Lancet.* 2006;368(9548):1673-9.

PubMed ID: 17098085

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The extended follow-up of the Finnish Diabetes Prevention Study was designed to assess the long-term results of the lifestyle intervention originally aimed at reducing the risk for developing type 2 diabetes in high-risk individuals.

Inclusion Criteria:

- Participant in the Finnish Diabetes Prevention Study.
  - Overweight (mean BMI = 31.1 kg/m^2)
  - Middle-aged (mean age = 55 yrs)
  - Impaired glucost tolerance

Exclusion Criteria:

- Individuals
  - not overweight
  - not middle-aged
  - not with impaired glucose tolerance

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Description of Study Protocol:

Recruitment

Recruited from 5 study centers in Finland.

Design

- Original study design: randomized controlled trial; intervention group with intensive diet-exercise counseling; control group.
- Post-intervention follow-up

Blinding used (if applicable): Implied for laboratory measures

Intervention (if applicable)

From the original design:

- Control group: given general verbal and written health behavior information at baseline without specific individualized advice.
- Intervention: intensive diet-exercise counseling with goals of: weight reduction of 5% or more; less than 30% of the daily energy intake from fat; less than 10% of the daily energy intake from saturated fat; fibre intake 15 g per 1000 kcal or more; and moderately intense physical activity 30 min per day or more. The duration of intervention ranged from less than 1 year up to 6 years, with median length of 4 years. Seven personal counseling sessions with the study nutritionist during the first year and every 3 months thereafter.

Post-intervention follow-up:

- All study participants had a yearly visit with the study nurse. The visits included the same procedures as during the intervention period, and were similar for all participants irrespective of their former randomization group. No specific diet or exercise counseling was provided.

Statistical Analysis

- Kaplan-Maier survival curves were calculated to estimate the probability of remaining free of diabetes in the two groups.Participants who were lost during follow-up were treated as censored observations. The difference between the survival curves was tested with the log-rank test.
- The Cox proportional hazards model was used to estimate the hazard ratio for development of diabetes. The proportionality assumption of the model was assessed with graphical methods (die, the log-log plot).
- All comparisons of the endpoints were based on the intention-to-treat principle.
- Mean levels of bodyweight, nutrient intakes, and physical activity during the study were compared between the groups with analysis of covariance, adjusting for the level of response variable at baseline.
- Further, analysis of covariance was used to examine changes in these variables from the last intervention period visit until the first post-intervention examination. In this analysis, adjustment was made for the level of respective variable at the last visit during intervention.
- In further analyses, the Cox model was used to analyze the relation between the success score and the incidence of diabetes. First, the success score variable was included in the model as categorical variable, with those who did not achieve any of the lifestyle goals as reference category. Additionally, test of linear trend was done including the success score as continuous variable in the model. In these analyses the groups were pooled.
- The analyses were adjusted for treatment group, study centre, sex, age, and the baseline 20h post-challenge plasma glucose concentration.

Data Collection Summary:

Timing of Measurements

- Randomization for the original study started in 1993 and was completed in 1998.
- The first interim analysis was done in March, 2000.
- End of intervention 2000-2001.
- Post-intervention follow-up in Dec, 2004.

Dependent Variables

- Development of type 2 diabetes was primary endpoint (defined using WHO 1985 criteria)
- Fasting and post load (75 g oral glucose tolerance test) plasma glucose after a 12-h fast.
- Body weight
- Proportion of physically active
- Energy proportion of fat (%)
- Energy proportion of saturated fat (%)
- Dietary fibre (g per 1000 kcal)
- Kaplan-Meier estimate of probability of remaining free of diabetes
- Success score: categorized according to their success in achieving the five predefined lifestyle goals (0=not achieved, 1=achieved) by the 3-year visit. A success score from 0 to 5 was calculated as the sum of the achieved goals. The analysis was repeated at the first post-intervention follow-up visit.

Independent Variables

- Intensive diet and weight counseling
- Weight reduction of 5%
- Total fat intake of <30% of energy
- Saturated fat intake <10% of energy
- Moderate daily physical activity of 30 min/day
- Increased fiber intake to >15 g/1000 Cal

Control Variables

Description of Actual Data Sample:

Initial N:

- Original study: 522 men and women in five study centres; intervention (n=265, the proportion of women 66%) or control (n=257, the proportion of women 69%).

Attrition (final N):

- Only followed those participants who were without diabetes at the end of the intervention.
- At the first post-intervention follow-up visit: intervention n=190; control n=165.
- The overall proportion of participants who were lost to follow-up was 10% in the intervention group and 8% in the control group (p=0.3619).

Age: mean age 55 years

Ethnicity: Finnish

Other relevant demographics: not given

Anthropometrics

Body weight at last intervention visit: intervention 81.8 kg; control 83.3 kg (p<0.0001)

First post-intervention follow-up visit: intervention 83.1 kg; control 84.0 kg (p=0.0032) test of equality between the groups, adjusting for baseline level; p=0.1482 test of equal change between the groups from the last intervention period visit to the first post-intervention follow-up visit, adjusting for the level at the last intervention visit.

Location: Five study centres, Finland

Summary of Results:

Key Findings

- The total number of cases of diabetes diagnosed during the overall follow-up of 7 years was 75 in the intervention group and 110 in the control group.
- The incidence rates were 4.3 (95% CI 3.4 - 5.4) and 7.4 (6.1 - 8.9) per 100 person-years in the intervention and control group, respectively (p=0.0001 log-rank test). The corresponding hazard ratio was 0.57 (0.43-0.76; as shown in Figure 2), indicating 43% reduction in relative risk.
- The cumulative incidence of diabetes at year 6 was 23% in the intervention group and 38% in the control group, with an absolute risk reduction of 15% (7.2 - 23.2).
- The number of people needed to be treated to prevent one case of type 2 diabetes by lifestyle intervention was 22 for 1 year.
- In the intervention and the control group, respectively, 10% and 27% of the participants did not achieve any of the predefined goals by the 3-year examination, whereas 14% and 6% achieved four or five goals (p<0.001).
- There was a strong inverse correlation between the success score and the incidence of diabetes during the total follow-up. Incidence rate per 100 person-years ranged from 8.4 (95% CI 6.2 - 11.3) in the participants who did not achieve any of the goals at the 3-year visit, to 2.0 (1.0 - 4.3) in those who achieved four or five of the goals. The hazard ratios were 1.00, 0.85 (0.57 - 1.28), 0.66 (0.40 - 1.09), 0.69 (0.38 - 1.26), and 0.23 (0.10 - 0.52) for success score from 0, 1, 2, 3, to 4-5, respectively (test for trend p=0.0004).
- The median post-intervention follow-up time was 3 years, and the number of incident new cases of type 2 diabetes was 31 in the intervention group of 221 people at risk, and 38 in the control group of 185 people at risk. The corresponding incidence rates were 4.6 and 7.2 per 100 person-years, respectively (log-rank test p=0.0401), ie, 36% relative risk reduction (as shown in figure 3).
- The differences in body weight, physical activity, and nutrient intakes between the groups remained favorable for the intervention group during the post-intervention follow-up. The proportion of physically active individuals decreased in the control group.
- In the intervention and control groups, respectively, 7% and 14% of the participants did not achieve any of the lifestyle goals at the first follow-up visit, 32% and 40% achieved one, while 18% and 7% achieved at least four out of the five goals (p=0.0042).
- The incidence rate of diabetes per 100 person years was 8.0 (95% CI 4.2 - 15.4) in the group that did not achieve any of the goals, compared with 3.8 (1.7 - 8.5) in the group with 4 or 5

goals achieved. The hazard ratios were 1.00, 0.96 (0.45 - 2.04), 0.37 (0.15-0.93), 0.78 (0.32-1.91) and 0.54 (0.20 - 1.49) for the success score from 0, 1, 2, 3, to 4 or 5, respectively (p=0.1089).

- Univariate hazard ratios (95% CI) for diabetes incidence during the post-intervention follow-up were 0.55 (0.30 - 1.02) for achieving the weight reduction goal, 0.74 (0.44-1.27) for achieving the fat intake goal, 1.01 (0.54-1.89) for achieving the saturated fat intake goal, 0.72 (0.40-1.30) for achieving the fibre intake goal, and 0.62 (0.36 - 1.06) for achieving the physical activity goal, compared with those who did not achieve the respective goal at the first post-intervention follow-up examination.
- When all five variables for lifestyle goals were simultaneously analyzed, the adjusted hazard ratios were 0.52 (0.28 - 0.96) for weight reduction from baseline, 0.67 (0.35-1.31) for the intake of fat, 1.62 (0.68-3.85) for the intake of saturated fat, 0.77 (0.38-1.57) for the intake of fibre, and 0.82 (0.46-1.48) for physical activity.

Author Conclusion:

Lifestyle intervention in people at high risk for type 2 diabetes resulted in sustained lifestyle changes and a reduction in diabetes incidence, which remained after the individual lifestyle counselling was stopped.

Reviewer Comments:

Limitations as stated by authors:

- *Can not distinguish between the carry-over effect from the intervention, and the ongoing effect of lifestyle during the post-intervention follow-up, on diabetes incidence.*
- *The analyses related to the post-intervention follow-up period were not planned in the original study protocol, and post hoc analyses have to be interpreted with caution. The post-intervention follow-up was not foreseen while calculating the original sample size, and because of low numbers of people at risk and cases of diabetes the statistical power remains restricted.*
- *The study participants were volunteers and willing to take part in a long-lasting trial and thus were probably more health-conscious than the general population.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes

4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes

4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A

7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes